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GRAVES' DISEASE AND ITS TREATMENT.

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There is no disease which shows so many signs of a universally acting toxemia as Graves' disease. Not a physiological function of the body escapes being characteristically disordered by it at some time or other during its chronic course. It is pertinent, therefore, at the outset of its consideration to ask what disease, toxic or otherwise, that can be named, approaches it in this respect? Thus the functional nervous symptoms include great nervousness; mental disturbances ranging from depression, aboulia, and changes of disposition to actual mania; distressing tinnitus which may end in complete deafness, to disappear, however, with recovery from the disease; all varieties of functional disorder of the eyes; affections of smell and of taste; pains general or peculiarly located, or limited to certain groups of muscles; headaches; vertigo; various parasthesiæ; local motor paralyses; bulimia; insomnia; and pruritus. The vascular symptoms include palpitation, enlargement and throbbing of the arteries, both general and local vasomotor paralyses, and the characteristic tachycardia. The muscular symptoms are tremors, either general or particularly local, general muscular debility, local weakness of the knees, weakness or spasm of the laryngeal muscles, cramp of the calves, abasia, etc. Disorders of nutrition appear in extreme emaciation with marked loss of bulk in muscles and in bones, loss of hair, and pigmentation. The glandular derangements show themselves by thyroid enlargement with exophthalmos, by severe and characteristic disorder of the gastric and intestinal secretions, and by sweating, not to mention irritability of the urinary bladder, with or without polyuria.

Every one of these derangements can be extreme in degree in individual cases, but however grave or even fatal some of them may be, yet they have one important feature in common, namely, that no organic change accompanies any one of them. In any other disease such severe symptoms would be sure to be due to, or sooner or later be accompanied by, either inflammatory or degenerative textural alterations; but not so in Graves' disease. The tachycardia, although marked and prolonged for years, is not caused by nor associated with carditis in any form, nor does the heart show any kind of degeneration different from the nutrition changes in other muscular tissues. In Graves' disease death often follows upon uncontrollable vomiting and diarrhœa, but autopsies of these cases reveal not a sign of gastritis or enteritis. No visible changes from the normal are found in the eyes nor in the ears, however seriously disordered functionally they may have been. Likewise the great irritability of the bladder has no cystitis to explain it, nor is the itching accompanied by any cutaneous eruption.

This proves that one and the same agent produces all the effects. Graves' disease, therefore, is one, and being so it cannot be confounded with anything else—an important fact to bear in mind when we find it with the name goitre attached to it; because most goitres have nothing to do with Graves' disease and produce none of its symptoms, nor, as we shall see, are other tissue changes in the thyroid, lately alleged to be distinctive of this complaint, really so, because they may be found on dissection without any preceding or accompanying signs of Graves' disease. On the other hand, nothing can be more certain than the diagnosis of Graves' disease itself, since no other malady has so many characteristic signs. The absence of some of them, such as exophthalmos or an appreciable enlargement of the thyroid, is more than made up by the presence it may be of twenty other symptoms which are thus particularly grouped only in this malady. Therefore, the only deduction possible is that the complaint is due to a specific poison which goes wherever the blood goes and which causes no more tissue changes, except, indirectly, on nutrition, than does opium or aconite.

What the nature and origin of this poison is remains wholly unknown. More than half a century ago, Dalton in the preface to his *Physiology* congratulated the profession on the prospect that Claude Bernard's recent discovery of the sugar-making function of the liver would soon reveal the cause of diabetes. At present the explanation of diabetes is not yet in sight. So, in 1902, Kocher printed a bibliography of 1400 books, treatises, and articles on Graves' disease, and since that time the list may be extended to

2500. But all the experimental research and clinical observation, to which this voluminous literature testifies, have served only to illustrate the manifold uncertainties connected with the subject itself, and where uncertainity abounds theories proliferate.

The chief cause of this uncertainity is that as correct physiology is an essential prerequisite to correct pathology, we are yet at sea as regards the physiology of the thyroid and its associated structures. Unlike the adrenals, the active principle of whose internal secretion has been isolated and even may be artificially constructed, no one knows what the internal secretion of the thyroid is. Undoubtedly one of its physiological uses is to prevent the myxœdema which supervenes upon atrophy or upon ablation of the gland, and which otherwise fatal disorder can be relieved by administration of thyroid extracts. But the inference of an indispensable function of the thyroid on this account is considerably modified by the fact that while this gland, like the thymus, is a temporary organ and goes out of commission after fifty years of age, myxœdema does not then follow either upon its atrophy or upon its surgical removal. Hale White,[1] Kocher,[2] and others have shown that as age advances the thyroid degenerates, and in old subjects the normal glandular structure can with difficulty be recognized. In dogs, if they are old, thyroidectomy is neither fatal nor accompanied by the usual symptoms. Kocher points out that postoperative myxœdema scarcely occurs at all in elderly people.

Bourneville and Bricon[3] put the limit to postoperative myxœdema as early as the thirtieth year. The thyroid, therefore, is needed for an ill-understood purpose connected with the age of the body, apparently corresponding with the duration of the reproductive functions, and which may have to do with the susceptibility of women, to Graves' disease, the ratio in my experience being 9 to 1 in men. But if Graves' disease is primarily a thyroid disease, especially if it be due, as supposed by many, to hypersecretion of the thyroid gland, how can we explain severe and even fatal cases of Graves' disease in elderly patients who seem to have no thyroid left? I treated a lady who, in the course of three years, had become dangerously reduced with exophthalmic goitre. After a year's treatment she apparently wholly recovered, having increased in weight from 81 pounds to 142 pounds, with disappearance of both the goitre and the exophthalmos, but three years subsequently she relapsed and died in her sixty-third year with all the symptoms of her original complaint, except that the thyroid seemed to be wholly atrophied and could not be felt. Another lady recovered for five years from the severest symptoms of Graves' disease, and then relapsed and died when she was sixty-five years old without a sign of goitre.

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[1] Lancet, 1888, i, 521.

[2] Arch. f. klin. Chir., 1883, xxix.

[3] Arch. de neurol., 1886.

On the other hand, much the commonest and most pronounced goitres have no connection or relationship with Graves' disease. This gland is very sensitive to certain as yet unidentified stimuli in drinking water which excite it to great overaction with consequent hypertrophy. Lombroso mentions a well in Lombardy whose water produces goitre in fifteen days, and is resorted to on that account by young men who thereby aim to escape military service. But how this gland may have its cells stimulated into such activity without developing from beginning to end a single one of the twenty-six peculiar symptoms of Graves' disease, is a question to which none of the advocates of undue "thyroidism" give a satisfactory answer. Moreover, all authorities concur in stating that Graves' disease is no more prevalent in localities where parenchymatous goitre is endemic than it is elsewhere.

In recent years the problem has been further much complicated by the inclusion of the parathyroids in its consideration. By some (Gley,[4] Vessale and Generale,[5] MacCallum[6] and others) the function of the parathyroids is regarded quite as essential to life as that of the thyroid itself, and hence all former discussions on Graves' disease in which the thyroid only was considered are deemed seriously defective. In rabbits the parathyroids are not embedded in the thyroids, and Gley's explanation why thyroidectomy seemed to cause so little effect in those animals was that the removal of that gland did not remove the parathyroids with it, but when he excised the parathyroids the full fatal train of nervous symptoms developed, though the thyroid was left intact. MacCallum's parathyroidectomies in dogs supported the same inference of the tetany, etc., being the result of the absence of the secretion of these glands. But other experimenters contradict their statements. Vincent and Jolly[7] in their recent reports deny that removal of the parathyroids has any effect in rats, guinea-pigs, and badgers, and state that monkeys showed only transient nervous symptoms after the operation, while nervous symptoms sometimes developed although these glands were left in situ.

But meantime if the parathyroids are all which is claimed for them the question still remains unsettled as to how much of the symptom-complex of Graves' disease can be attributed to hypo- or to hyper-secretion of these little bodies or to total absence of their secretion owing to their entire disappearance, as this has been reported in examinations both of the thyroids of fatal cases and in thyroids removed by surgical operations.

Another of the many anomalies of this complaint is the supervention after surgical operations on the thyroid of two very serious conditions which are quite distinct in their nature from each other, although often confounded together. The first, which is almost uniformly fatal, is the development in the course of some hours after operation of rapidly increasing hyperpyexia rising from 103° F.. to 108° F. or 110° F., with great dyspnœa, extreme tachycardia, pulmonary œdema, coma, and death. Formerly this was called "acute thyroidism" and ascribed to sudden absorption of thyroid secretion from vessels and surfaces cut in the operation, or to undue handling of the gland, dislodging quantities of the secretion into the circulation. But it would be difficult to bring together so many pure assumptions as this view does or where theory and facts are so wide apart. That the thyroid should contain a powerful thermic poison at any time is rendered improbable by the clinical fact that the most fatal effects of the toxemia of Graves' disease continue to the last in keeping with all its other manifestations, in that no fever accompanies them. Graves' disease is preëminently a non-febrile complaint. In the second place this same fatal condition takes place after operations for Graves' disease in which the thyroid has not been cut into at all, and when every precaution was taken not to disturb it. R. F. Curtis,[8] alarmed by three deaths from "acute thyroidism" out of 11 thyroidectomies performed by him, tried instead the operation of sympathectomy in 7 patients, and although in operating he carefully avioded either wounding or handling the thyroid, 2 out of the 7 died from this imaginary thyroidism.

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[4] Compt.-rend. Soc. de biol., 1891.

[5] Arch. Ach. ital de Biol., 1895.

[6] Trans. Assoc. Amer. Phys., xviii, 35.

[7] Jour. Physiology, 1905, xxxi; 1906, xxiv.

A more probable explanation of this condition, so indicative of profound bulbar disturbances from the heat centre to the cardiorespiratory centres, is furnished by the intimate relations of the cervical sympathetic and of the thyroid itself to the medulla, section of the restiform bodies producing permanent exophthalmos. In fact it is dangerous to disturb the bulbar centres with any afferent excitation wholly new to them. Over 40 deaths with all the hyperpyexia and other symptoms of alleged acute thyroidism have been published as following upon washing out the pleura, and several from washing out the stomach, one of which, in the Addenbrook Hospital, London, was exactly parallel in onset and course with those following thyroidectomy.

The other condition has been called postoperative tetany, and although occasionally fatal, in some cases becomes chronic with symptoms characteristic of the disorder long known under the name tetany. This affection is itself obscure enough on account of its developing in the course of so many widely different diseases. It occurs in a variety of infections including malaria, but especially in gastro-intestinal disturbances, in teething infants, in nursing women, in Bright's disease, etc. But when the fact is added that its prevalence may be both endemic or epidemic, discussion of its etiology ceases to be practicable. Nevertheless the symptoms attending its development after operations on the neck are so similar to those following experimental parathyroidectomy that a good case may be made out for ascribing it then to trauma of those glandules or to interference with their blood supply. Halsted's[9] postoperative case, which in time was greatly improved by the administration of the parathyroids of beeves, strongly supports this view. Meanwhile, R. L. Thompson[10] in his exhaustive paper on *Atrophy of the Parathyroid Glandules in Primary Infantile Atrophy*, remarks that he never met with tetany in such infants and that the histological investigation of these glandules is in general negative in cases which had tetany in life, the records as usual being very contradictory, so that the fact is by no means proved that in the human subject destruction of these bodies always produces tetany.

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[8] Trans. Amer. Surg. Assoc., 1903.

The very latest pronouncement on this subject is by Dr. David Forsyth,[11] who by grants from the Royal Society and from the Science Committee of the British Medical Association, was enabled to make the most extensive experimental researches on parathyroids in all kinds of mammalia, as well as in birds. He expresses as his final conclusions the opinion that the parathyroids are glands not necessary to life and are essentially thyroidal in nature and possess no peculiar function.

Recently much interest has been awakened by the reports of Beebe and John Rogers of the successful treatment of Graves' disease by hypodermic injections of an antitoxin prepared from thyroids of cases of exophthalmic goitre. There can be no question of the apparently beneficial, if not the curative, effects of this new method of treatment in some cases, but its explanation is another matter. I can conceive that the specific poison of Graves' disease may be especially accumulated in the substance of the hypertrophied gland so that from it an antitoxin can be manufactured after the usual methods. This serum treatment, however, failed in two cases of my own although faithfully administered, by one of its discoverers for several weeks to the first patient, and similar failures have been reported by others. This, however, is only in keeping with other "cures" of Graves' disease, early enthusiasm subsiding with more experience.

But the most serious objection to the view that Graves' disease is primarily due to hypersecretion by the thyroid lies in the occurrence of numerous cases of Graves' disease, some of them fatal, in which there was no goitre or exophthalmos at any time in their history. It is begging the question to call such cases non-typical, *fruste*, or abortive when they show all the typical symptoms of the malady except goitre and exophthalmos, and equally so is it to term them latent or incomplete when the disease runs its course to a fatal issue in as large a proportion with them as in those with goitre. In my monograph on *Graves' Disease With or Without Goitre*[12] I give the detailed histories of 68 patients: 41 with goitre and 27 without, with a careful comparison of the percentage of each symptom in the two classes, sufficient to demonstrate that there could be no mistake in the diagnosis of the cases without goitre as nevertheless undoubted examples of Graves' disease. In this list there were 2 deaths among those with goitre, and 2 also in the lesser number without goitre. Not one of these 68 patients was a hospital case, because though I have had many such, yet their stay in hospitals is too short to make observations on them satisfactory, particularly as to the effects of any measures for treatment, medical or surgical. I have had 4 patients who seemed perfectly recovered from the disease, in 3 of them for periods of three, four, and five years, and then die from a relapse of the original complaint. The fourth who had not consulted me for nearly seven years because he said that at no time had he been ill, then relapsed and came very near dying, although he has since measurably recovered. Everyone of those patients had resumed a meat diet.

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[9] AMER. JOUR. MED. SCI., July and October, 1907.

[10] Ibid., October, 1907.

[11] Quarterly Jour. Medicine, January, 1908.

Since the publication of that monograph, I have had a number of other cases of both classes, in private and in consultation practice, and I now regard those without goitre as on the whole the more difficult to treat. One lady without any goitre, whose mother died from Graves' disease, has been continuously under my observation for eighteen years with severe recurrences of Graves' disease whenever she takes meat. She had a sister who presented the same symptoms without goitre for five years and then developed a pronounced goitre just as she was getting well. She was very confortable with her goitre for six months, after which it wholly disappeared. Two years afterward she succumbed to cancer of the breast. Graves' disease goitre is very changeable in its size without any reference to the other symptoms, so that I pay but little attention to it.

Prof. Barker,[13] however, is seemingly so convinced that Graves' disease is necessarily a thyroid disease, that if we do not find a goitre there must be something of the kind nevertheless, and that faulty examination is responsible for the failure to find these virulently poisonous masses. He admits, however, that he has had three cases in his hospital wards in whom no such growth was palpable. But to me his views seem influenced by the observations of MacCallum and Halsted of a definite kind of alteration in thyroid tissue in Graves' disease, the anatomical details of which may be found in MacCallum's paper.[14] These changes may involve the whole gland or be limited to certain foci, when, of course, clinicians may be wholly ignorant of them and of their significance. I can only say that clinicians would welcome any anatomical proofs of Graves' disease and long have been waiting for them. But when Dr. MacCallum adds that these same textural appearances, general and local, may be found in the thyroids of sheep, goats, and particularly in stray dogs, and Dr. A. Kocher[15] says in human thyroids also, without any of the symptoms of Graves' disease accompanying them, these anatomical peculiarities may really have no more causative relationship to Graves' disease than the goitres produced by the waters of Lombroso's wells. Graves' disease without general indistinction from local symptoms does not exist, and as to foci I do not believe that a single focus remained in the atrophied thyroids of the two old ladies above mentioned, who died with all the symptoms of Graves' disease and of no other disease.

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[12] William Wood & Co., New York, 1904.

[13] Jour. Amer. Med. Assoc., October 12, 1907.

[14] Ibid., October 5, 1907.

I was early led to question the view that this malady is caused exclusively hy hypersecretion of thyroid juice, because like Pompey's Pillar at Alexandria this theory is so striking by its solitariness. If true it would tower over the whole field of medicine quite alone. We are all acquainted with hypersecretion by glands, but never without our being able to account for this behavior of theirs either by the presence in the blood of something which excites them, or less frequently by some nervous irritation. Salivation, however common, is never due to the parotids spontaneously flowing. As to a nervous irritation causing a serious morbid process persisting unchanged it may be for years, this, as Fagge well remarks, is a phenomenon wholly unknown in pathology. There is no limiting theorizing when the nervous system is brought in, as when Hector Mackenzie ascribes Graves' disease invariably to fright, so that although the patient cannot remember the fright some ancestor of hers may once have been badly scared and thus started the process. Hence I pay little credence either to the view that Graves' disease comes from the cervical sympathetic or that the thyroid secretes its poison just as it were, from its own innate depravity. If the thyroid does secrete uncommonly, something not of the thyroid must make it do so. This doubt, however, by no means excludes the supposition that when once Graves' disease is established by its own primary cause, conditions of the thyroid and of the sympathetic may materially affect its course.

My own views of the pathology, and, therefore, of the treatment of Graves' disease, are based upon therapeutics. Clinical observations are as good as laboratory experiments, provided that in making them the same care is taken against fallacies in observation and in deduction. This cannot be done without writing down the observations every time they are made, through years if necessary. Only private, in distinction from hospital, patients, for reasons already stated, will afford the necessary data for conclusive demonstration.

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[15] Jour. Amer. Med. Assoc., October 12, 1907.

My final verdict is that proper medical treatment furnishes the best chances for recovery from the disease in *severe* cases, and, of course, therefore, in the milder forms. If I could have the complete control of the management of the patient I would prefer one who has been brought too low by the disease for the surgeon to venture to propose operation. The histories of several such are detailed in my book. Incipient or mild cases too often improve spontaneously to be at all conclusive. The one condition when I would have but little hope is when uncontrollable vomiting and diarrhœa have supervened in a patient already far gone. As the best cure for indigestion is digestion the only recourse then is to find some form of food which will stay down although only in very small doses. At no time in the course of Graves' disease can its diarrhœa be checked by opiates or by astringents.

As to pathology, my first surmise of it was suggested by the case of a lady who came to me with exophthalmic goitre twenty-seven years ago, much reduced in flesh and strength. In addition to medical prescriptions which I now regard as useless, although found then in the text-books, I enjoined her restriction to the Asiatic fermented milk preparations, which I was the first to introduce to this country, but which are quite generally used now under the names of kumyss, matzoon, zoolak, etc. She immediately began to improve in every respect, and after six months felt so well that she ceased her visits. In three months more I was called to see her again prostrated with her old symptoms. Again she was put on the milk and again she thought she had recovered. At the end of another summer I was hastily summoned to her bedside only to feel her pulse stop forever while I had my finger on it. I was told by her family that in spite of their protests she began to eat meat heartily, saying that she would rather die than take the milk. Similar injury to patients with this disease from indulgence in butcher meat has been duplicated in my experience ever since. I would as soon recommend confirmed diabetics to take all the starchy food they please, as to advise the Graves' people to relieve their weakness with that strengthening article, roast beef.

Here it begins to look like discerning the same relations of Graves' disease to the nitrogenous elements of food that diabetes has to the starchy elements, in other words we find our therapeutic guide (diet) leading us directly into the great forest of metabolism where all paths are soon lost in the thick undergrowths of theory. But what we do know is that in diabetes, if the system cannot get any carbohydrates it will split up its proteins into sugar with fatal results, and hence in Graves' disease our proper dieting must somehow provide nitrogen the best way it can, and for that we will give a diet list accordingly. But how about those glands in the neck? Some say that if the parathyroids are removed a virulent poison soon destroys the dogs unless they are freely bled and a compensatory amount of normal saline is infused, when they will live for twenty-four hours until this same poison has accumulated enough to necessitate a repetition of the infusion. Or the dogs may be kept longer alive if they are fed on bread and water. Give them meat and it quickly kills them. The plain deduction is that a poison coming from somewhere is normally neutralized by the parathyroids, and the effect of diet points to the alimentary canal as the source of the poison. The steps between the food taken and the parathyroids belong to the yet hidden secrets of metabolism, and so also do the other problems of Graves' disease, for the whole symptom-complex of this malady cannot be explained by the parathyroids. One other poison at least must be accounted for, whose property is to paralyze the vasoconstrictors everywhere, and by dilating all arterioles cause the tachycardia and many of the other symptoms of the disease. This poison, therefore, is the opposite of adrenalin in its effects.

But we are now again landed in the thickets of theories. One theory has long held the field, namely, that whereas the parathyroids neutralize a poison the larger gland produces one, or what is virtually so by its own proper secretion being improperly increased. Oswald, however, insists that instead of its own secretion being increased it is decreased. However, not to prolong an article already suggestive of why there are 2500 other writings on this subject, we will call in our therapeutics to supply a theory based on a solid fact to begin with, which is that by proper diet Graves' disease generally subsides as commonly as glycosuria after middle life disappears by its proper diet. In addition to this some of its most intractable symptoms promptly yield to medicines which affect the intestines. Repeatedly I have brought down the pulse forty beats by one blue pill, which certainly cannot slow the pulse in the same way that veratrum viride does, because neither veratrum nor any other cardiac sedative controls this tachycardia. Hence it may be that a poison generated in the alimentary canal normally finds in the thyroid what the other poison finds in the parathyroids, that is, a gland which can neutralize it. Excessive amounts of this poison in the blood excite the thyroid into overaction and thus often, not always, lead to its hypertrophy. The goitre, therefore, is secondary to a blood condition, just as hypertrophy of the spleen is, and to get rid of it and of all its other accompaniments we must attend to the intestine.

All theories, however, that I know of about Graves' disease have one failure in common, viz., that no one of them explains all the facts, and mine outlined above is no exception. How a toxemia originating in the alimentary canal can be cured by a surgical operation not on the alimentary canal but on the thyroid, is not very clear. That Graves' disease has been successfully relieved or cured by such operations is no longer to be questioned. My only answer is that it seems to me equally clear that the theory of Graves' disease being primarily and always a thyroid disease is a mistaken theory, and, hence, that the seeming contradiction is because the whole subject abounds with anomalies, as do all problems connected with metabolism, not the least of which is to explain on what surgical principle the present mode of operating in Graves' disease is based, as we will soon note.

We do not yet know much of the physiology of metabolism. Thus the relations of the internal secretions of the little islands of Langerhans to diabetes are no plainer than those of the little parathyroids to fatal tetany. We are yet to learn what enzymes are and what they do. Nor have we yet learned all about antitoxins ar antibodies. Sometimes a chemical process is supposable and at others equally inadmissible. My own provisional hypothesis in this case is that, due to a physiological affinity the thyroid may accumulate a store of enzyme-like toxin brought to it by the circulation which may then act as a nidus for discharging the agent from time to time when the gland is stimulated by fresh supplies of the toxin derived from improper diet. Surgically removing this nidus may then be as beneficial as removal of the spleen sometimes is when it has hypertrophied from noxious accumulations in its substance. But neither this nor any other hypothesis yet offered covers the whole ground. A complete thyroidectomy would be the only recourse if the usual explanation of the benefits of the operation was valid. Instead, at present, only partial resections are recommended. The part of thyroid left, no matter how diseased, then becomes normal as does the patient also. This surgical fact has no parallel elsewhere, certaintly not in the infections or degenerations dealt with by surgeons. Neither a tuberculous gland nor a patch of gangrene can be left to get well, because it has been half cut out. A cure of such a serious toxemia as that of Graves' disease by removing a portion only of the thyroid gland is beyond all present explanation, and can be accepted merely as an empirical fact.

But it is also a fact that Graves' disease, whatever its stage or degree, can be equally benefited or cured by proper medical treatment alone. Failure then is due to difficulty in managing the patient and not the disease. Many women seem incapable of that perseverance in observing the regimen and continuing the medication for the prolonged time that is essential to control a malady which is like diabetes in its requirements for both abstinence and observance. One of the important objects is to enjoin rest from muscular exertion, to secure which the physician should explain to the patient that muscular debility is a specific accompaniment of the affection as much so as in fever, and no transient condition which will-power can overcome. But likewise all fatigue is to be avoided. It is striking how soon certain nervous symptoms, such as headache and insomnia, follow upon both undue muscular and mental exertion in these patients.

On the matter of diet the directions cannot be too positive and too detailed. Butcher meat is never to be allowed. Fish, if not too oily, as salmon or smelts, seems much less objectionable than meat. Oysters, clams, and lobsters are forbidden. Poultry can be taken sparingly, but not at night. Not more than one egg a day, best taken at breakfast, is allowable. Of game I only allow quail and partridge, but no dark meat birds.

The standard article, however, is milk, which alone will cure many severe cases of Graves' disease if it be taken as the Bedouins and Tartars of Asia take it as well nigh their only food. A Bedouin would no more drink fresh milk than we would eat a raw potato. He always ferments it first, with yeast as the ferment. Most Tartars use the plant keffir as their ferment. Peptonized milk will answer if the patient does not know how to make the fermented milk. Raw milk, on the other hand, is wholly indigestible in the quantities which should be taken in this disease, and if ever taken should be half diluted with Vichy or with lime-water.

Next to living on milk the patient should be a vegetarian, for vegetable albumen rarely disagrees. Bread, particularly if crusty, and rice can be taken ad libitum, but hot soda biscuits are nearly poisonous, and starchy crackers are to be avoided in persons much troubled with headaches. Of vegetables, beans (except string beans) and peas are wholly inadmissible. I would rule out also asparagus and, to a less degree, spinach. Of the cereals oatmeal is forbidden, but the others in common use, particularly hominy, are recommended as they are so often taken with milk and cream. Nearly all the fruits are beneficial except uncooked apples and strawberries. Of course in a disease so marked with digestive disturbances, individual idiosyncracies will have to be respected.

Medicinal treatment holds a high place in my estimation. To every patient I recommend 30 grains of the phosphate of sodium taken at the beginning of each meal. A blue pill or other mercurial laxative taken twice a week is a routine prescription. Then a course of intestinal antiseptics is kept up for months at a time. I usually begin with sodium salicylate and sodium benzoate, of each 10 grains, an hour after each meal. At bedtime I give a capsule containing naphthalene 3 grains and sodium benzoate 6 grains. After a time I substitute a capsule containing phenol bismuth and ammonium benzoate, each 5 grains, of which two should be taken an hour after meals. The principle of these remedies as intestinal antiseptics being understood, every physician can vary the prescriptions as he finds best.

No patient with confirmed Graves' disease should be promised a speedy cure. I once thought that two years' absence of all its symptoms might allow the hope that it would not return, but I do not now, because my experience makes me dread a case of relapse after a long interval of freedom more than I do any other instance of the disease. I have mentioned the patients who, once severely affected with Graves' disease, apparently remained entirely well for periods varying from three to seven years. They then relapsed and none of the remedial measures which before were so effective were of any avail; four out of the five dying on my hands. This result is not without its analogy in diabetes, for if a diabetic once indulges in starches his glycosuria then increases often for weeks after his indiscretion, though he may have quickly returned to his old observance of rules of abstinence; and as I have mentioned above each of my patients with a late relapse had returned to a meat diet.

ADIPOSIS TUBEROSA SIMPLEX.

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There is a condition which resembles Dercum's disease in respect to certain clinical features, but it differs markedly from adiposis dolorosa in its course, and, unlike the latter disease, is amenable to treatment. The subjects are obese and sometimes extremely so, as in one case which I observed. The disorder may occur in the plethoric or the anemic form of obesity, although more commonly perhaps in the latter.

Circumscribed fat masses appear in the subcutaneous tissues; they form distinct, moderately dense, slightly movable, somewhat flattened tumors, ranging in size from a bean to that of a hen's egg. Their number varies all the way from one-half dozen to two dozen or more. These moderately firm fat-nodules are not distributed over the entire body, but in some cases are confined to the extremities, particularly the lower, and in others, to the abdomen. The tumor masses show no tendency to fuse together and are not elevated above the surrounding surface; they are sensitive to the touch and may be the seat of pain which varies in intensity within rather wide extremes, being moderately severe and distressing in rare cases and trivial or even absent in the majority of instances. The lymphatic glands are not involved, and the skin remains soft, flexible, and non-adherent. The mental processes are normally active, and also the muscles; asthenia is not present, and there is no more indisposition to physical exertion than is observed in cases of obesity as a rule. The knee-jerks are present and the cutaneous sensibility is unaltered, in some cases at least. The mammæ and abdominal panniculus adiposis may be overhanging or pendulous, but not in all cases, as an analysis of the symptoms of the instances reported below will indicate. It is